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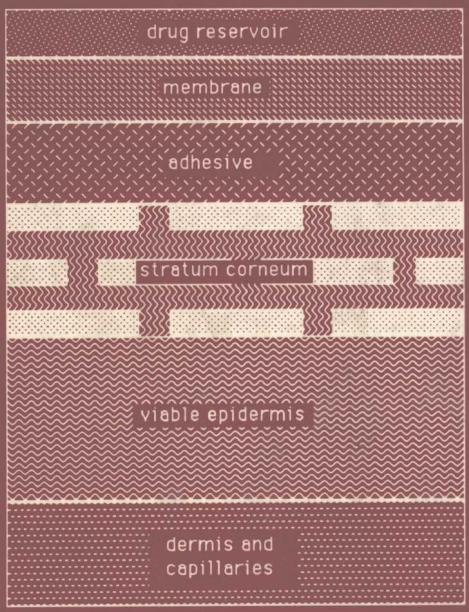
Transdermal Drug Delivery

Developmental Issues and Research Initiatives



edited by
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Transdermal Drug Delivery

Developmental Issues and Research Initiatives

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Transdermal Drug Delivery

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Preface

Pharmaceutical knowledge has grown exponentially over the last 25 years. We now have a much clearer understanding of how drugs are absorbed into, distributed within, and cleared from the body. The potency of the agents with which we deal continues to increase, and our ability to unravel mechanisms of action proceeds. New drug entities—in particular peptides, proteins, and other biological response modifiers—are being developed and new challenges await the pharmaceutical scientist. Controlled drug delivery represents a field that must keep pace with the changing nature of chemotherapy. Tighter control of drug input into the body in both quantitative and temporal senses is crucial, and the fabrication of delivery systems must respond to this demand for increased sophistication.

Transdermal delivery has become an important means of drug administration. The number of investigators in this area has undergone a dramatic expansion and multiple symposia have focused on the subject. In this flurry of activity, developmental projects were established with little recognition of the inherent problems associated with chemical transport across the skin. As a result, several of these fledgling investigations have foundered. It is our belief that many of the problems encountered could (and should) have been foreseen. In some cases, the difficulties may not have been solvable; in others, we suspect, solutions were available but escaped attention because the problem was incompletely understood.

The first objective of this book is to highlight those key issues to which attention must be paid during the *early* stages of transdermal delivery system development. The subsequent aim is to indicate areas in which important progress is occurring and further basic research is needed. The contributors to this text have been

directed to emphasize the problems involved in percutaneous drug delivery and to describe rational approaches to circumvent such hurdles. Our authors were selected for their depth of knowledge and reputation in their subject areas, and for their ability to address objectively, without false optimism or uninformed pessimism, the topics of this book. We believe that they have performed this task effectively, producing a text that will facilitate and optimize future developmental programs in transdermal drug delivery.

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Transdermal Drug Delivery

Contents

1

Stratum Corneum: Biological and Biochemical Considerations

PHILIP W. WERTZ and DONALD T. DOWNING *University of Iowa College of Medicine, Iowa City, Iowa*

I. INTRODUCTION

"Indeed, the *raison d'être* of the epidermis is to make the stratum corneum; this is its specific biologic mission." (1)

In order to fully understand the form and function of the stratum corneum it is helpful to know the processes involved in its formation from the living cells of the epidermis. Traditionally, several layers of living cells, constituting the Malpighian region, have been named either for their location or their appearance: the strata basale, spinosum, and granulare. The dead cells of the stratum corneum form the stratum lucidum (or compactum) and the stratum disjunctum. Although these terms or their English equivalents are still used, it is important to realize that the entire architecture of the epidermis constitutes a dynamic system in which each cell changes continuously during its passage from the basal layer where it is formed to the surface of the horny layer where it is discarded.

Study of the epidermis includes the morphology of the changing cell types, the dynamics of the differentiation process, the arrangement and chemical composition of the subcellular structures, the metabolic processes occurring in epidermal cells, and the location, composition, and physical properties of the epidermal barrier. All of these are discussed in this chapter as a basis for evaluating the physical and pharmacological aspects of transdermal drug delivery.